What is claimed:

1. A method for preparing a protein-polymer conjugate comprising:
(a) contacting an insulin protein with a hydrophilic polymer in the presence of at least one organic solvent and at least one metal chelator, under conditions that promote the formation of a conjugate of the protein and the polymer; and
(b) isolating the conjugate.

2. The method of claim 1, wherein the insulin protein comprises human insulin.

3. The method of claim 1 or 2, wherein the hydrophilic polymer is selected from the group consisting of polyethylene glycol, polyethylene glycol/polypropylene glycol copolymers, polyoxyethylated glycerol, and linear, branched and amino-reactive derivatives thereof.

4. The method of claim 3, wherein the amino-reactive derivative is selected from the group consisting of an aldehyde, a N-hydroxy succinimide, a PNP-carbonate, and a benzotrizole terminated hydrophilic polymer.

5. The method of any of the preceding claims, wherein the hydrophilic polymer and insulin protein are contacted at a molar ratio of about 10:1-1:1.

6. The method of any of the preceding claims, wherein the organic solvent is selected from the group consisting of ethanol, methanol, DMSO, dioxane, DMF, and NMP.

7. The method of any of the preceding claims, wherein the organic solvent is present at a concentration of about 0.1 to 10%.

8. The method of any of the preceding claims, wherein the insulin protein and hydrophilic polymer are contacted at a protein concentration of about 0.1-5.0%.

9. The method of any of the preceding claims, wherein the insulin protein and hydrophilic polymer are contacted at a pH of about 5.0-7.5.

10. The method of any of the preceding claims, wherein the chelator is selected from the group consisting of polyvalent metal ion chelators, EDTA, deferoxamine (DEF), diethylenetriamine pentaacetic acid (DTPA), and bis(aminoethyl)glycolether N,N,N',N'–tetraacetic acid (EGTA).

11. The method of any of the preceding claims, wherein the chelator is present at a concentration of about 0.1-10 mM.

12. The method of any of the preceding claims, wherein the insulin protein and hydrophilic polymer are contacted at a temperature of about 4-50° C.

13. The method of any of the preceding claims, wherein the method further comprises the step of quenching formation of the conjugate prior to isolating the conjugate.

14. The method of claim 13, wherein the quenching is achieved by reducing the pH to about 1-4.

15. The method of any of the preceding claims, wherein the isolation is achieved by chromatography.

16. The method of claim 15, wherein the chromatography comprises ion exchange chromatography.

17. The method of any of the preceding claims, further comprising the step of encapsulating the conjugate in a biodegradable polymer.

18. A method for preparing an insulin-PEG conjugate comprising:

(a) contacting insulin with PEG in the presence of at least one organic solvent and at least one metal chelator, under conditions that promote the formation of a conjugate of the insulin and PEG; and

(b) isolating the conjugate.

19. The method of claim 18, wherein the insulin comprises human insulin.

20. The method of claim 18 or 19, wherein the PEG comprises an amino-reactive PEG derivative selected from the group consisting of an aldehyde, a N-hydroxy succinimide, a PNP-carbonate, and a benzotrizole terminated hydrophilic polymer.

21. The method of any one of claims 18-20, wherein the PEG and insulin are contacted at a molar ratio of about 10:1-1:1.

22. The method of any one of claims 18-21, wherein the PEG and insulin are contacted at a protein concentration of about 0.1-5.0%.

23. The method of any one of claims 18-22, wherein the PEG and insulin are contacted at a pH of about 5.0-7.5.

24. The method of any one of claims 18-23, further comprising the step of quenching formation of the conjugate prior to isolating the conjugate.

25. The method of claim 24, wherein the quenching is achieved by reducing the pH to about 1-4.

26. The method of any one of claims 18-25, wherein the isolation is achieved by ion exchange chromatography.

27. The method of any one of claims 18-26, further comprising encapsulating the conjugate in a biodegradable polymer.